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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,230	10/13/2000	Sylvia Braselmann	ONYX1027-DIV1	1176

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	17

DATE MAILED: 05/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/687,230	BRASELMANN, SYLVIA	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-12 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 8-12 and 23 are pending.

Applicant's amendment of claims 8-11, addition of claim 23 and amendments to the specification in Paper No. 16, filed on 4/3/2003 are acknowledged.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/3/2003 has been entered.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Priority

1. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/030,103 filed on 11/01/1996.

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 08/942,008 filed on 10/01/1997.

Claim Objections

3. Claim 8 is objected to because of the recitation of "SH2". Abbreviations unless otherwise obvious and/or commonly used in the art, should not be recited in the claims without

at least once reciting the entire phrase for which the abbreviation is used. It is suggested that the term "src homology 2" be inserted before the term SH2. Appropriate correction is required.

4. Claim 9 is objected to because of the recitation of "protein of claim 8 wherein a bromodomain comprises amino acids...". For clarity, it is suggested that the term be amended to recite "protein of claim 8 wherein amino acids ....of SEQ ID NO: 2 encode a bromodomain" or similar. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 8-12 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 8 (claims 9-12 dependent thereon) is indefinite in the recitation of "binds to the intermediate SH2 domain on the regulatory subunit of phosphatidylinositol-3' kinase by the associated protein(s) C-terminal amino acids" for the following reasons. As written, it is unclear if the C-terminus of several proteins binds to the intermediate SH2 domain. It is suggested that the claim be amended to recite "an isolated phosphatidylinositol-3' kinase associated protein comprising the polypeptide of SEQ ID NO: 2, wherein the C-terminal amino acids of said phosphatidylinositol-3' kinase associated protein bind to the intermediate SH2 domain of the regulatory subunit of phosphatidylinositol-3' kinase" or similar. For examination purposes, the suggested language will be used. Correction is required.

8. Claim 23 is indefinite in the recitation of "nucleotide sequence which hybridizes under stringent conditions to the nucleotide sequence..." for the following reasons. First, it is unclear as to how a sequence can hybridize to another sequence since hybridization occurs among molecules. Sequences as known in the art, are graphical representations of the order in which nucleotides/amino acids are arranged in a molecule. It is suggested that the claim be amended to recite "an isolated....protein encoded by a polynucleotide which hybridizes....to the polynucleotide of SEQ ID NO: 1". In addition, the term "stringent conditions" is indefinite absent a statement indicating the actual hybridization/wash conditions. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. It is noted that the specification discloses at least two types of "stringent conditions", highly stringent and moderate stringent, therefore it is unclear as to which "stringent" conditions are being referred to. It is suggested that if Applicant's intended conditions are highly stringent, the claims be amended to recite the experimental conditions for the hybridization/wash reactions as indicated in page 10, lines 34-35. For examination purposes, the term "stringent conditions" will be interpreted as "any conditions". Correction is required

Claim Rejections - 35 USC § 112, First Paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 23 is directed to a genus of phosphatidylinositol-3' kinase associated proteins encoded by polynucleotides which can hybridize under any conditions to the polynucleotide of SEQ ID NO: 1. See claim rejections under 35 USC 112, second paragraph for claim interpretation. While the specification discloses the structure and function of the polypeptide of SEQ ID NO: 2 and the corresponding polynucleotide (SEQ ID NO: 1), the specification fails to describe the structural elements required in polynucleotides which can hybridize under any conditions to the polynucleotide of SEQ ID NO: 1 in order to encode phosphatidylinositol-3' kinase associated proteins. An adequate description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. The recited structural feature of the genus (i.e. polypeptide encoded by a polynucleotide which can hybridize under any conditions to the polynucleotide of SEQ ID NO: 1) does not constitute a substantial portion of the genus since the remainder of the structure of any phosphatidylinositol-3' kinase associated protein is completely undefined and the specification does not provide the remaining structural features necessary for members of the genus to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

11. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2, does not reasonably provide

enablement for any phosphatidylinositol-3' kinase associated protein which is encoded by a polynucleotide which hybridizes under any conditions to the polynucleotide of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claim is not commensurate with the enablement provided by the disclosure for the following reasons. While Applicants have disclosed the function and structure of the polypeptide of SEQ ID NO: 2, the specification does not provide any information as to which are the structural elements a polynucleotide which can hybridize under any conditions to the polynucleotide of SEQ ID NO: 1 should have to encode a phosphatidylinositol-3' kinase associated protein.

While one could argue that adequate enablement has been provided for the proteins of the instant claims since one can isolate these proteins by sequence comparison using the polynucleotide/polypeptide structures disclosed in the instant application or the prior art, the state of the art teaches that sequence comparison alone should not be used to determine function and that small structural changes can drastically change the function of a polypeptide. Bork (Genome Research, 10:398-400, 2000) teaches protein function is context dependent, and both

molecular and cellular aspects must be considered (page 398). Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to be hydroxylases once tested for activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Since amino acid structure determines function, one would require some knowledge or guidance as to how structure correlates with function to isolate the claimed polypeptides. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to display the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate those polypeptides, as encompassed by the claim, Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Double Patenting

12. Claims 9 and 10 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 8. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, the polypeptides of claim 9 and 10 are the same as that of claim 8 since in all cases, the claimed polypeptide must comprise the amino acid sequence of SEQ ID NO: 2.

Conclusion

13. No claim is in condition for allowance.

14. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

15. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
May 1, 2003

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~
1600